

CLAIMS

1. An isolated nucleic acid molecule selected from the group consisting of
 - (a) a nucleic acid molecule which hybridizes under stringent conditions to a molecule having a nucleotide sequence selected from the group consisting of the nucleotide sequence of
5 SEQ ID NO:4 and the nucleotide sequence of SEQ ID NO:6, wherein the isolated nucleic acid molecule codes for a LAGE-1 tumor associated polypeptide,
 - (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to the degeneracy of the genetic code, and
 - (c) complements of (a) and (b), wherein the isolated nucleic acid molecule excludes
10 nucleic acid molecules having the nucleotide sequence of SEQ ID NO:8.
2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:4.
- 15 3. The isolated nucleic acid molecule of claim 2, wherein the isolated nucleic acid molecule comprises the coding region of the nucleotide sequence of SEQ ID NO:4.
4. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:6.
- 20 5. The isolated nucleic acid molecule of claim 4 wherein the isolated nucleic acid molecule comprises the coding region of the nucleic acid sequence of SEQ ID NO:6.
6. The isolated nucleic acid molecule of any of claims 1, 2 or 4, wherein the isolated nucleic
25 acid molecule comprises an allelic variant of a LAGE-1 nucleic acid molecule.
7. An isolated nucleic acid molecule selected from the group consisting of:
 - (a) a unique fragment of nucleotides 1-993 of SEQ ID NO:4 between 12 and 992
nucleotides in length,
 - 30 (b) a unique fragment of nucleotides 1-746 of SEQ ID NO:6 between 12 and 745
nucleotides in length,
 - (c) complements of "(a)", and

(d) complements of "(b)", wherein the unique fragment excludes nucleic acid molecules which consist only of fragments of SEQ ID NO:8.

8. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 14 contiguous nucleotides.

9. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 15 contiguous nucleotides.

10. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 16 contiguous nucleotides.

11. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 17 contiguous nucleotides.

12. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 18 contiguous nucleotides.

13. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 20 contiguous nucleotides.

14. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is at least 22 contiguous nucleotides.

15. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule is between 12 and 32 contiguous nucleotides.

16. The isolated nucleic acid molecule of claim 7, wherein the isolated nucleic acid molecule comprises at least 5 contiguous nucleotides not present in SEQ ID NO:8.

17. An expression vector comprising the isolated nucleic acid molecule of any of claims 1-16 operably linked to a promoter.

18. A host cell transformed or transfected with the expression vector of claim 17.

19. The host cell of claim 18, wherein the host cell expresses an HLA molecule.

20. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 1, 2, 3, 4, 5 or 6.

21. The polypeptide of claim 20, wherein the polypeptide has an amino acid selected from the group consisting of the amino acid sequence of SEQ ID NO:5, the amino acid sequence of SEQ ID NO:7, the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:7 having a glutamine to arginine substitution at residue 6, the amino acid sequence of SEQ ID NO:5 or SEQ ID NO:7 having a glutamine to glutamic acid substitution at residue 89, and the amino acid sequence of SEQ ID NO:5 having an arginine to tryptophan substitution at residue 138.

22. An isolated LAGE-1 polypeptide comprising amino acids 89-93 of SEQ ID NO:7.

23. The isolated LAGE-1 polypeptide of claim 22, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of amino acids 71-93 of SEQ ID NO:7, 71-98 of SEQ ID NO:7, 89-98 of SEQ ID NO:7, 89-111 of SEQ ID NO:7, and 71-111 of SEQ ID NO:7.

24. An isolated LAGE-1b polypeptide comprising an amino acid sequence selected from the group consisting of amino acids 142-148 of SEQ ID NO:5, amino acids 187-205 of SEQ ID NO:5, and amino acids 164-179 of SEQ ID NO:5.

25. The isolated LAGE-1b polypeptide of claim 24, wherein the polypeptide comprises amino acids 134-210 of SEQ ID NO:5.

26. An isolated polypeptide selected from the group consisting of:
(a) unique fragments of SEQ ID NO:5 between 9 and 209 amino acids in length, and
(b) unique fragments of SEQ ID NO:7 between 9 and 179 amino acids in length, wherein

the unique fragment excludes polypeptides consisting of fragments of SEQ ID NO:9.

27. The isolated polypeptide of claim 26, wherein the unique fragment binds to a polypeptide-binding agent.

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28. The isolated polypeptide of claim 27, wherein the polypeptide-binding agent is an antibody or a cytotoxic T lymphocyte.

29. An isolated polypeptide which selectively binds a protein encoded by the isolated nucleic acid molecule of claim 1, 2, 3, 4, 5 or 6.

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30. The isolated polypeptide of claim 29, wherein the isolated polypeptide is an Fab or F(ab) fragment of an antibody.

31. The isolated polypeptide of claim 29, wherein the isolated polypeptide is a fragment of an antibody, the fragment including a CDR3 region selective for the protein.

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32. The isolated polypeptide of claim 29, wherein the isolated polypeptide is a monoclonal antibody.

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33. A kit for detecting the presence of the expression of a tumor associated polypeptide precursor comprising a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of nucleotides 1-993 of SEQ ID NO:4, (b) a 12-32 nucleotide contiguous segment of nucleotides 1-746 of SEQ ID NO:6, (c) complements of "(a)", and (d) complements of "(b)", wherein the contiguous segments are nonoverlapping.

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34. The kit of claim 33, a wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify the isolated nucleic acid molecule of claim 1.

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35. The kit of claim 34, a wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify a portion of both SEQ ID NO:4 and SEQ ID NO:6.

36. The kit of claim 33 wherein the pair of isolated nucleic acid molecules is PCR primers, wherein one of the primers is a contiguous segment of SEQ ID NO:4 and another of the primers is the complement of a contiguous segment of SEQ ID NO:4.

5 37. The kit of claim 33 wherein the pair of isolated nucleic acid molecules is PCR primers, wherein one of the primers is a contiguous segment of SEQ ID NO:6 and another of the primers is the complement of a contiguous segment of SEQ ID NO:6.

38. A method for diagnosing a disorder characterized by expression of a LAGE-1 nucleic acid molecule or an expression product thereof, comprising:
10 contacting a biological sample isolated from a subject with an agent that selectively binds the isolated nucleic acid molecule of claim 1 or an expression product thereof, and
determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

15 39. The method of claim 38 wherein the agent is a nucleic acid molecule comprising SEQ ID NO:4 or SEQ ID NO:6, or a unique fragment thereof.

40. The method of claim 38 wherein the interaction is determined by amplifying at least a
20 portion of the nucleic acid molecule.

41. The method of claim 38 wherein the agent is a cytolytic T lymphocyte.

42. The method of claim 38 wherein the agent is an antibody or antibody fragment.

25 43. A method for treating a subject with a disorder characterized by expression of a LAGE-1 tumor associated polypeptide, comprising

administering to the subject an amount of an agent which enriches selectively in the subject the presence of complexes of a HLA molecule and a tumor rejection antigen derived
30 from a LAGE-1 tumor associated polypeptide coded for by a nucleic acid molecule as described in claims 1, 2, 3, 4, 5, or 6, sufficient to ameliorate the disorder.

44. The method of claim 43, wherein the agent is the isolated polypeptide of any of claims 20, 22, 24 and 26, or an immunogenic fragment thereof.

45. A method for treating a subject with a disorder characterized by expression of a LAGE-1 nucleic acid molecule or an expression product thereof, comprising:

administering to the subject an amount of autologous cytolytic T cells sufficient to ameliorate the disorder, wherein the cytolytic T cells specific for complexes of an HLA molecule and a LAGE-1 tumor associated polypeptide or an immunogenic fragment thereof.

46. The method of claim 45, wherein the LAGE-1 tumor associated polypeptide is the polypeptide of any of claims 20, 22, 24 and 26.

47. A method for treating a subject with a disorder characterized by expression of a LAGE-1 nucleic acid molecule or an expression product thereof, comprising:

administering to the subject an amount of a LAGE-1 tumor associated polypeptide or an immunogenic fragment thereof sufficient to ameliorate the disorder.

48. The method of claim 47, wherein the LAGE-1 tumor associated polypeptide is the polypeptide of any of claims 20, 22, 24 and 26.

49. A method for enriching selectively a population of T cells with cytolytic T cells specific for a LAGE-1 tumor associated polypeptide comprising:

contacting an isolated population of T cells with an agent presenting a complex of a LAGE tumor associated polypeptide or an immunogenic fragment thereof and a HLA presenting molecule in an amount sufficient to selectively enrich the isolated population of T cells with the cytolytic T cells.

50. The method of claim 49 wherein the LAGE-1 tumor associated polypeptide is the isolated polypeptide of any of claims 20, 22, 24 and 26.

51. The method of claim 49 wherein the agent is a cell which expresses a LAGE-1 tumor associated polypeptide and a HLA molecule.

52. The method of claim 51, wherein the LAGE-1 tumor associated polypeptide is encoded by a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:4 or SEQ ID NO:6.
53. A vaccine composition comprising a nucleic acid encoding LAGE-1 or an immunogenic fragment thereof.
54. A vaccine composition comprising a LAGE-1 polypeptide or an immunogenic fragment thereof.
55. A vaccine composition comprising a cell which expresses a LAGE-1 nucleic acid or polypeptide, or an immunogenic fragment thereof.
56. An isolated nucleic acid molecule which encodes the polypeptide of any of claims 22-25.